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ORIGINAL ARTICLE

Left Ventricular Mass is Preserved in Patients with Idiopathic Pulmonary Arterial Hypertension and Eisenmenger's Syndrome

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Background Left ventricular (LV) atrophic remodelling was described for chronic thromboembolic pulmonary hypertension (PH) but not in other forms of PH. We aimed to assess LV morphometric changes in idiopathic pulmonary arterial hypertension (IPAH) and Eisenmenger's syndrome(ES).

Methods Fifteen patients with IPAH, 15 patients with ES and 15 healthy volunteers were included. Magnetic resonance was used to measure masses of LV, interventricular septum (IVS), LV free wall (LVFW), and LV end diastolic volume (LVEDV) indexed for body surface area.

Results Between patients with IPAH, ES and controls no differences in $LVmass_{index}$ (54.4[45.2-63.3] vs 58.7 [41.5-106.1] vs 52.8[46.5-59.3], p = 0.50), $IVSmass_{index}$ (21.6[18.2-21.9)] vs 27.4[18.0-32.9] vs 20.7[18.2-23.2], p = 0.18), and $LVFWmass_{index}$ ([32.4[27.1-40.0] vs 36.7[30.9-62.1] vs 32.5[26.9-36.1], p = 0.29) were found. $LVEDV_{index}$ was lower in IPAH patients than in controls and in ES patients (54.9[46.9-58.5] vs 75.2[62.4-88.9] vs 73.5[62.1-77.5], p < 0.001). In IPAH LVEDV but not LV mass correlated with pulmonary vascular resistance (r = -0.56, p = 0.03) and cardiac output (r = 0.59, p = 0.02).

Conclusions LV mass is not reduced in patients with IPAH and with ES and is not affected by haemodynamic severity of PH. LVEDV is reduced in IPAH patients in proportion to reduced pulmonary flow but preserved in patients with ES, where reduced pulmonary flow to LV is compensated by right-to left shunt.

Keywords Left ventricular hypotrophy • Cardiovascular magnetic resonance • Left ventricular volume

Introduction

Left ventricular (LV) diastolic and systolic dysfunction have been reported to accompany chronic pressure overload of the right ventricle (RV) and correspond with poor outcome [1–3]. They have also been considered a potential mechanism of pulmonary oedema in the course of restoration of the pulmonary flow after lung transplantation [4,5] in patients with pulmonary hypertension (PH).

The mechanisms underlying LV dysfunction in the course of PH are not fully understood and among the others an atrophic remodelling of LV has been proposed [6]. It is

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assumed that a reduced flow through the pulmonary circulation leads to a reduced LV preload and LV unloading and consequently to a reduction in LV mass [6].

Recently, it was shown that in patients with chronic thromboembolic PH (CTEPH) and RV systolic dysfunction the LV free wall (LVFW) mass was lower than in healthy volunteers [6]. The exact mechanisms of the observed reduction in LVFW mass are still unclear: Apart from chronic mechanical unloading of LV it has also been speculated that factors released from the diseased pulmonary circulation might be involved in the LV remodelling [7].

Up to now, the phenomenon of atrophic remodelling of the human LV in PH has been described only in CTEPH [6]. However, different aetiologies of elevated pulmonary artery pressure seem to result in differential effects on the RV [8,9] and thus maybe also on the LV. Idiopathic pulmonary arterial hypertension (IPAH) is similar to CTEPH with respect to haemodynamic impact on the RV and LV, but the different pathophysiologies in the pulmonary vascular bed might also have different effects on LV remodelling. Eisenmenger's syndrome, where unloading of the LV due to reduced inflow from the pulmonary circulation is diminished by right-to-left shunt, represents a completely different haemodynamic situation.

Therefore, we aimed to assess morphometric changes of the LV in two different aetiologies of PH namely IPAH and Eisenmenger's syndrome.

Patients and Methods

Study population

Between June 2009 and September 2012, 61 patients diagnosed with IPAH and Eisenmenger's syndrome at the Department of Cardiac and Vascular Diseases at John Paul Hospital in Krakow, Poland, were eligible to be included into a study program aimed to characterise the populations and to determine the prognostic factors of disease progression. The study protocol comprised right heart catheterisation in all patients and cardiovascular magnetic resonance (CMR) in patients with sinus rhythm. From this study program we selected two groups of patients: 1) 15 consecutive patients with IPAH and 2) 15 age and sex matched patients with Eisenmenger's syndrome. Inclusion criteria for both patient groups were age 18 to 55 years and sinus rhythm. Main exclusion criteria were current or previous prescription of PAH specific drugs, presence of coronary artery disease (exclusion by coronary angiography), the presence of main risk factors for atherosclerosis (hypertension, hypercholesterolaemia, diabetes, smoking) and contraindications to CMR.

In addition, 15 age and sex matched healthy volunteers were recruited and underwent CMR imaging. The institutional ethics committee approved the study protocol, and informed consent was obtained from each participant before enrolment. The study conforms to the ethical guidelines of the 1975 Declaration of Helsinki.

Study protocol

Data on medical history, and laboratory parameters were obtained and CMR was performed in all participants. Right heart catheterisation (RHC) was performed according to the current recommendations [10] in all patients with pulmonary hypertension. Cardiovascular disease risk factors were assessed according to the current guidelines [11–14]. Body mass index (BMI) was calculated as weight [kg]/height [m]^2. CMR was performed no longer than three days after RHC in which the diagnosis of IPAH or Eisenmenger's syndrome was established. Coronary angiography was performed to exclude coronary artery disease.

Cardiovascular Imaging

Breath-hold, ECG-gated magnetic resonance imaging was performed using cardiac-phased array coil on 1.5 T whole-body scanner (Magnetom Sonata Maestro Class, Siemens, Erlangen, Germany) in LV and RV short-axis and axial views. After scout imaging, cine imaging (steady-state free precision gradient echo technique; slice thickness 8 mm, no gap, matrix 256 × 192, in-plane resolution 1.3 × 1.3 mm^2) was acquired. Cine images were assessed off-line (MASS Medis, Leiden, the Netherlands) by independent, experienced observers blinded to other data. Endocardial and epicardial borders were outlined on short axis images as previously described [15–17]. Mass of the LV free wall (LVFW) and interventricular septum (IVS) were measured separately. The LVFW extends from RV-LV junction in the anterior wall to the RV-LV junction in the inferior wall [6]. Myocardial mass was determined by multiplication of the tissue volume by 1.05 g/cm^3 (specific density of myocardium). LV and RV end-diastolic volume (EDV), and end-systolic volume (ESV) were measured by outlining endocardial and epicardial RV and LV borders, and stroke volume (SV), cardiac output (CO), and ejection fractions (EF) were calculated. All CMR parameters except for LV EF were indexed for body surface area (BSA) and only indexed values were used for further analysis. LV mass index and LVEDV index of study participants were compared not only with controls but also with previously published reference values [17]. In order to put the LV mass in relation to the degree of LV unloading we calculated the LV mass to volume ratio: LV M/V = LV mass (g)/LVEDV(ml) [18]. Right ventricular systolic dysfunction was defined as CMR-derived RV ejection fraction <45% [6].

To assess the potential influence of abnormalities in interventricular septal motion at end-diastole on LVEDV in patients with IPAH we measured the eccentricity index using echocardiography (Vivid 7 GE Medical System). It was measured by the parasternal short-axis at the level of the ventricular papillary muscles as the ratio of the minor axis of LV parallel to the septum, divided by the minor axis perpendicular to the septum according to the current standards [19].

Statistical analysis

Continuous variables were reported using median and interquartile range, categorical variables as counts and percentages.